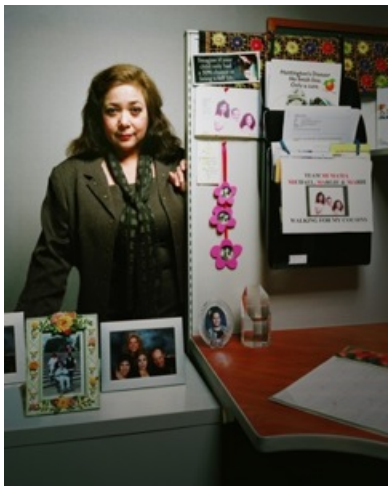
Stories of Hope: Huntington's Disease



Margie Hayes takes a small, graceful and unintended dance step as she follows her mother. She is the only one of **Frances Saldaña**'s three children who can still walk, who can still accompany her mother to public events to talk about the disease devastating their family.

Saldaña's youngest daughter, Marie Portillo, 31, is in hospice. Her 36-year-old son, Michael Portillo, is in a care facility unable to walk. Their father died of Huntington's disease 18 years ago. And Margie, 38, is no longer allowed to drive as her symptoms worsen. This is the legacy of Huntington's disease.

Frances Saldaña met Hector Portillo when she was 13 and he was 16. There were whispers that disease ran in his family, but he said no. He didn't show symptoms until after their youngest was born. All three children carry the Huntington's mutation.

"The heart break does set in, but I don't allow it," Saldaña says. "I just tell myself, don't go there. I surround myself with really positive and brilliant people who are going to make this the last generation with Huntington's disease."

Stem cells will play an essential role in that wish, she said. "It's the only hope for a treatment right now."

- Watch the Spotlight on Huntington's Disease talks
- Read more about CIRM funding for Huntington's disease research

Curing Huntington's Disease

On the short arm of our fourth chromosome we have a stuttering gene. Repeatedly, it instructs the creation of the amino acid glutamine.

For most of us, the gene will repeat the instruction fewer than 27 times. But in a few families the code repeats 36 times, 45 times, 100 times. And in this repetition, Huntington's disease is born.

Although the gene that pulls this wicked prank was identified in 1993, little is known about how the errant protein it makes induces uncontrolled dancelike movements, loss of cognitive ability, mood swings and death. "It's the worst aspects of Parkinson's disease, Alzheimer's and ALS [amyotrophic lateral sclerosis] all rolled into one," said Robert Pacifici, PhD, the chief scientific officer for the private non-profit CHDI Foundation, which is looking for potential Huntington's treatments.

In most genetic diseases, children are at risk only if both parents carry the deleterious mutation. But the Huntington's mutation is a dominant trait, meaning that each child has a 50/50 chance of carrying the fatal mutation and developing the disease if only one parent has it.

The malformed protein has its biggest impact on the medium spiny neurons, a group of branching cells that make 90 percent of the

brain's corpus striatum. But how these neurons die isn't clear. "We know medium spiny neurons are most affected, but we don't know if it's murder or suicide," Pacifici says. Until such details are figured out, drug developers work in the dark, uncertain just what to target.

Hans Keirstead, PhD, co-director of the Sue and Bill Gross Stem Cell Research Center at the University of California, Irvine, is creating populations of stem cells with the Huntington's genetic mutation to help answer some of those questions.

"It amazes me that no such stem cell lines exist right now. Not a one in the entire world," Keirstead said. With the advent of pre-implantation genetic testing, in which couples can screen embryos for disease genes before undergoing in vitro fertilization, there are now embryos with Huntington's disease markers available. Keirstead has arranged for fertility clinics to send him embryos with markers for Huntington's and other diseases.

But stem cells without mutations hold yet another promise. Keirstead's laboratory can coax them to become medium spiny neuron progenitor cells. Ultimately, such cells may be able to replace the neurons targeted in Huntington's."That's the beauty of the strategy," Keirstead said. "You rely on the cells themselves."

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